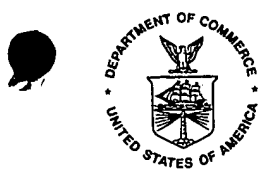

UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/614,003	07/11/00	GEHRING	W 7326-092

020583
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NEW YORK NY 10036-2711

HM12/0615

EXAMINER	
GANSHEROFF,L	
ART UNIT	**PAPER NUMBER**
1636	4

DATE MAILED: 06/15/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/614,003	GEHRING ET AL.	
	Examiner	Art Unit	
	Lisa Gansheroff	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-69 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claims 1-69 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15)☐ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18)☐ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☒ Other: *detailed action* .

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1, 2, 3, 7, 9, 10, 24-31, 32-33, 34, 50-52, 63-66, 69, drawn to a method of altering cell fate comprising contacting the cell *in vitro* with or administering to an organism an agonist of Notch pathway function and an agonist of a cell fate control gene pathway function, classified in class 435, subclass 377.

II. Claims 1, 2, 4, 8, 9, 10, 21, 24-31, 32-33, 34, 50-52, 63-66, 69, drawn to a method of altering cell fate comprising contacting the cell *in vitro* with or administering to an organism an agonist of Notch pathway function and an antagonist of a cell fate control gene pathway function, classified in class 435, subclass 377.

III. Claims 1, 10, 13, 14, 18, 20, 21, 24-31, 32-33, 34, 50-52, 63-66, 69, drawn to a method of altering cell fate comprising contacting the cell *in vitro* with or administering to an organism an antagonist of Notch pathway function and an agonist of a cell fate control gene pathway function, classified in class 435, subclass 377.

IV. Claims 1, 13, 15, 19, 20, 21, 24-31, 32-33, 34, 50-52, 63-66, 69, drawn to a method of altering cell fate comprising contacting the cell *in vitro* with or administering to an organism an antagonist of Notch pathway function and an antagonist of a cell fate control gene pathway function, classified in class 435, subclass 377.

V. Claims 35, drawn to a method of treating a patient by administering to the patient cells produced by the method of claim 34, classified in class 424, subclass 93.1.

VI. Claims 36, 38, 39, 40, 41 drawn to a method of treating macular degeneration comprising agonizing Notch pathway function in retinal pigment epithelium or retinalneuroepithelium of the patient, classified in class 514, subclass 2 or 44.

VII. Claims 37, 38, 39, 40, 41, 42, 43, 44 drawn to a method of treating macular degeneration comprising agonizing Notch pathway function in retinal pigment epithelium or retinalneuroepithelium of the patient, and agonizing Pax6 pathway function, classified in class 514, subclass 2 or 44.

VIII. Claim 45, drawn to a method of changing the cell fate of a mature cell type *in vitro* or in an organism comprising contacting the cell with an antagonist of Notch pathway function, then agonizing Notch pathway function and contacting the cell with an agonist of cell fate control gene pathway function, classified in class 435, subclass 377.

IX. Claim 45, drawn to a method of changing the cell fate of a mature cell type *in vitro* or in an organism comprising contacting the cell with an antagonist of Notch pathway function, then agonizing Notch pathway function and contacting the cell with an antagonist of cell fate control gene pathway function, classified in class 435, subclass 377.

X. Claims 46, 47, 48, 49, drawn to a kit comprising a molecule that is an agonist of Notch pathway function and a molecule that alters a cell fate control gene pathway, classified in class 435, subclass 377.

XI. Claims 46, 48, drawn to a kit comprising a molecule that alters Notch pathway function but is not an agonist, and a molecule that alters a cell fate control gene pathway, classified in class 435, subclass 377.

XII. Claim 53, 55, 57, 60, 61, 69, drawn to a method for altering cell fate *in vitro* or in an organism comprising contacting the cell with an agonist of Notch pathway function and subjecting the cell to conditions while maintaining the alteration to Notch pathway function, classified in class 435, subclass 377.

XIII. Claim 53, 56, 57, 60, 61, 69, drawn to a method for altering cell fate *in vitro* or in an organism comprising contacting the cell with an antagonist of Notch pathway function and subjecting the cell to conditions while maintaining the alteration to Notch pathway function, classified in class 435, subclass 377.

XIV. Claims 54, 55, 57, 60, 61, drawn to a method for producing an organ of a different type comprising contacting cells *in vitro* with or administering to an organism an agonist of Notch pathway function and subjecting the cells to conditions that allow organ differentiation until an organ is produced classified in class 435, subclass 1.1.

XV. Claims 54, 56, 57, 60, 61, drawn to a method for producing an organ of a different type comprising contacting cells *in vitro* with with or administering to an organism an antagonist of Notch pathway function and subjecting the cells to conditions that allow organ differentiation until an organ is produced classified in class 435, subclass 1.1.

XVI. Claim 58, drawn to a method of treating a patient by administering to the patient cells of a particular cell fate produced according to the method of claim 53, classified in class 424, subclass 93.1.

XVII. Claim 59, drawn to a method of treating a patient by administering to the patient an organ of a particular type produced according to the method of claim 54, classified in class 424, subclass 93.1.

XVIII. Claim 62, drawn to a method for producing an organ comprising an agonist or antagonist of Notch pathway function and an agonist or antagonist of a cell fate control gene pathway function, classified in class 435, subclass 1.1.

XIX. Claim 67, drawn to a method for screening, comprising altering a cell fate control gene pathway function and contacting the cell with or expressing within the cell test agonists or antagonists of Notch pathway function, classified in class 435, subclass 4.

XX. Claim 68, drawn to a method for screening, comprising altering Notch pathway function and contacting the cell with or expressing within the cell test agonists or antagonists of cell fate control gene pathway function, classified in class 435, subclass 4.

Some claims have been placed into more than one Group. Each claim that has been placed into multiple groups is generic to those groups and will be examined only to the extent it reads on the elected Group.

The following are further elections required upon election of certain Groups. The following are all different Inventions:

Upon election of **any Group**, Applicants must further elect the type of agonist and/or antagonist to be used as one of the following: a nucleic acid, a protein, or any other type of agonist/antagonist disclosed in the specification. The Group will be examined only to the extent that it reads on the type of agonist/antagonist elected, as each is a different Invention. In the case, for example, of claim 8 (and any similar claims) in which the agonist and antagonist appear to be expression products of nucleic acids that are introduced into the cell, Applicants should clearly indicate what the invention is: for example, is the antagonist a protein, with the method comprising introducing the nucleic acid into the cell to express the protein, or is the antagonist a nucleic acid such as, for example, an "antisense" molecule that is expressed from the introduced nucleic acid, and so forth. (Note also that antibodies are distinct from other types of proteins).

Each of the following Groups drawn to cell fate control gene pathway function: **I-V, VIII-XI, XVIII-XX**, is generic to patentably distinct cell fate control genes. Upon election of any of these Groups, Applicants must also elect one cell fate control gene (for example, one of those recited in the claims or one disclosed in the specification) to be examined with the elected Group. That is, one gene is to be elected, not a family of genes such as genes encoding "a homeodomain protein" which comprises distinct genes of different functions. Each cell fate control gene represents a distinct Invention.

Group V (claim 35) is generic to a method comprising producing cells by patentably distinct steps recited in claim 34, and then administering the cells to a patient. Upon election of Group IX, Applicants must also elect from the following: whether the cells are produced with (i) an agonist of Notch or (ii) with an antagonist of Notch; and whether the cells are produced (A) with an agonist of a cell fate control gene pathway function or (B) with an antagonist of a cell fate control gene pathway function. That is, Applicants must elect a set of i or ii plus A or B. Each set (for example: i, A) is a different Invention.

Groups XVI (claim 58), **XVII** (claim 59), and **XVIII** (claim 62) are each generic to methods comprising different sets of steps. Upon election of either Group XVI or Group XVII, Applicants must also elect from the following: whether the method is performed (i) with an agonist of Notch or (ii) with an antagonist of Notch. Additionally for Group XVIII, Applicants must also elect whether (A) an agonist of a cell fate control gene pathway function, or (B), an

antagonist of a cell fate control gene pathway function is to be used. That is, Applicants must elect a set of i or ii (plus A or B, if Group XVIII is elected). Each set (for example: i, A) is a different Invention.

The inventions are distinct, each from the other because of the following reasons:

Inventions VI and VII are related as combination and subcombination. Inventions in this relationship are distinct if it can be shown that (1) the combination as claimed does not require the particulars of the subcombination as claimed for patentability, and (2) that the subcombination has utility by itself or in other combinations (MPEP § 806.05(c)). In the instant case, the combination as claimed does not require the particulars of the subcombination as claimed because the combination (VII) of agonizing both the Notch and Pax6 pathways could be patentable as a method of treating macular degeneration. The subcombination (VI) has separate utility such as treating macular degeneration without the need for agonizing Pax6 pathway function.

Inventions X and XI, which are kits, are related to the Inventions that are methods as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the kits could be used for a variety of distinct methods claimed in the different method Groups, and thus are not

particular to one method. Further, the molecule in the kits that alters Notch pathway function can be used on a different cell from the molecule that alters cell fate control gene pathway, so that two cells are affected independently by the molecules of the kits.

Invention XVI is related to Inventions XII-XIII as combination and subcombination. Inventions in this relationship are distinct if it can be shown that (1) the combination as claimed does not require the particulars of the subcombination as claimed for patentability, and (2) that the subcombination has utility by itself or in other combinations (MPEP § 806.05(c)). In the instant case, the combination as claimed does not require the particulars of the subcombination as claimed because the treatment method (the combination) could be patentable because of the treatment effects. The subcombination has separate utility such as for laboratory research to study cell fate control gene pathways.

Invention XVIII is related to Inventions XIV-XV as combination and subcombination. Inventions in this relationship are distinct if it can be shown that (1) the combination as claimed does not require the particulars of the subcombination as claimed for patentability, and (2) that the subcombination has utility by itself or in other combinations (MPEP § 806.05(c)). In the instant case, the combination as claimed does not require the particulars of the subcombination as claimed because the treatment method (the combination) could be patentable because of the treatment effects. The subcombination has separate utility such as for laboratory research to study cell fate control gene pathways in organ development or to prepare organ tissue for biochemical research.

Invention XVIII and XIV-XV are related as combination and subcombination. Inventions in this relationship are distinct if it can be shown that (1) the combination as claimed does not require the particulars of the subcombination as claimed for patentability, and (2) that the subcombination has utility by itself or in other combinations (MPEP § 806.05(c)). In the instant case, the combination as claimed does not require the particulars of the subcombination as claimed because the combination of agonizing both Notch pathway and cell fate control gene pathway function could be patentable as a way of preparing an organ. The subcombination has separate utility such as preparing an organ without the need for agonizing or antagonizing cell fate control gene pathway function.

Inventions I-IX and XII-XX are unrelated (except in the cases of combination/subcombination discussed above). Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are methods that comprise steps not present in or not required for the other methods.

For example, some of the methods use agonists of Notch pathway function, while others use antagonists; the effects of agonists and antagonists are opposite and thus the effects of the methods would be distinct. Likewise, methods that use agonists of cell fate control gene pathway function comprise a different step and have different effects from methods that use antagonists of cell fate control gene pathway function. Some methods use both an antagonist and

an agonist of Notch pathway function, with the steps being in a particular order (VIII-IX), and thus these methods are distinct in steps and effect from methods using only an agonist or an antagonist of Notch pathway function. Any art involving compositions with effects on the Notch or a cell fate control gene pathway would have to be evaluated for whether the effect was agonistic or antagonistic. For example, art that taught altering cell fate with a compound that agonized the Notch pathway would not necessarily teach that the same result could be achieved with a compound that worked in an exactly opposite way (an antagonist).

The different treatment methods (VI, VII, XVI, and XVII) recite different steps from each other, and are different from other methods because a treatment effect is obtained, and the method is performed on a particular type of organism (one needing said treatment).

Methods that produce organs (XIV-XV) are distinct in steps (such as providing conditions for organ differentiation to occur) and effect from methods that produce cells without requiring production of an organ.

Screening methods for agonists/antagonists of Notch pathway (XIX) or for agonists/antagonists of cell fate control gene pathway (XX) function are distinct from other methods because in screening methods, the compounds tested are not yet identified as agonists or antagonists, while the other methods require the use of compounds already known to be agonists or antagonists.

Different cell fate control genes are structurally (by sequence) and functionally different from each other, as some are transcription factors, some are signaling molecules, and transcription factors act at different promoters, in different cell types, and have different function; likewise cell fate control genes that are not transcription factors also have different

structures and functions from each other and from each transcription factor. Thus, the methods (or kits) as drawn to different cell fate control genes are patentably distinct independent inventions.

Finally, since proteins are distinct chemically, biologically, and functionally from nucleic acids, and since proteins and nucleic acids are chemically, biologically, and functionally distinct from any other type of molecule that might be used as an agonist or antagonist, protein agonists/antagonists are patentably distinct from nucleic acid agonists/antagonists, and so forth.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper. Further, examination of the groups together would present a severe burden on the Examiner. The searches for the different groups not be coextensive, and the evaluation of the search results would depend upon the group.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the

application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa J. Gansheroff whose telephone number is (703) 605-1203. The examiner can normally be reached 9 AM - 5 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached at (703) 308-0447. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242 for regular communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst Dianiece Jacobs whose telephone number is (703) 305-3388 or to the receptionist whose telephone number is (703) 308-0196.

LG
June 1, 2001

JAMES KETTER
PRIMARY EXAMINER